

**P20 at UT Southwestern**

**Taskforce for Obesity  
Research at Southwestern  
(TORS)**

**Jay D. Horton, MD**  
**UT Southwestern Medical Center at Dallas**

# **Response to P20 Mandate**

- **Taskforce for Obesity Research at Southwestern-TORS**
  - **Build and expand existing strengths at UTSW to develop an interdisciplinary approach to the study of obesity and components of the metabolic syndrome**

# **Biological Problem –**

## ***Obesity and the Metabolic Syndrome***

- **Obesity in U.S.**
  - **31% obese (BMI>30)**
  - **65% overweight (BMI>25)**
- **Metabolic Syndrome**
  - **Atherogenic dyslipidemia**
  - **Type 2 Diabetes Mellitus**
  - **Hypertension**
  - **Hepatic Steatosis**

# Texas Adults - The Facts

- **Obesity:**
  - African- Americans= 42%
  - Hispanics= 30%
  - All Texas Adults= 25%
- **Obesity and overweight:**
  - Men (69%)
  - Women (55%)
  - 45-64 years of age (70%)

# Goals

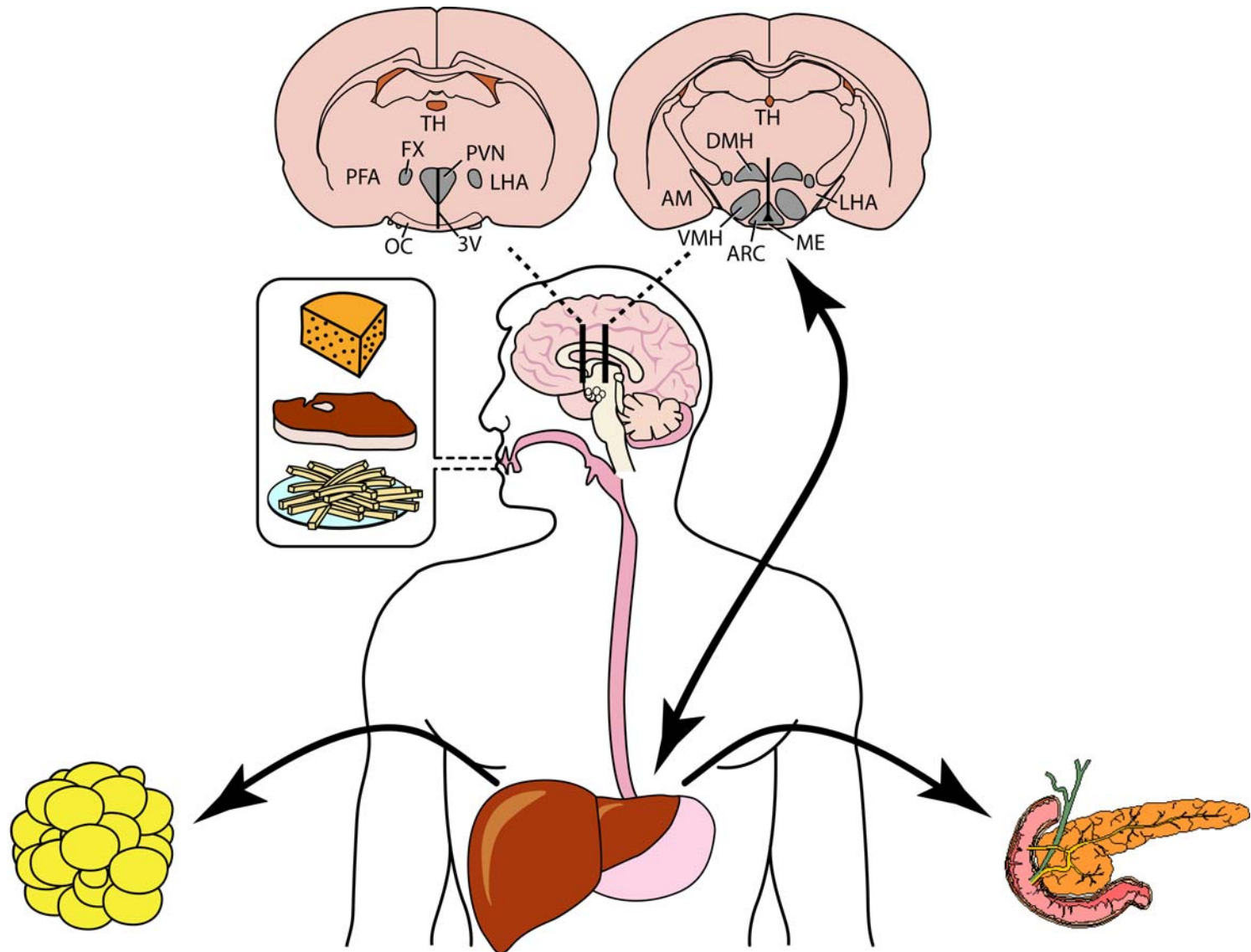
- **Immediate Goals**

- Elucidate molecular mechanisms in brain that regulate food intake and energy homeostasis
- Determine how dysregulation of glucose and lipid metabolism in the liver affects obesity and components of the metabolic syndrome

- **Long-term Goals**

- Create a comprehensive obesity and metabolic disease program
- Develop directed approaches to prevent obesity and treat its metabolic complications

# ***Initial Focus: Brain-Liver Interactions in Obesity and the Metabolic Syndrome***



# Implementation

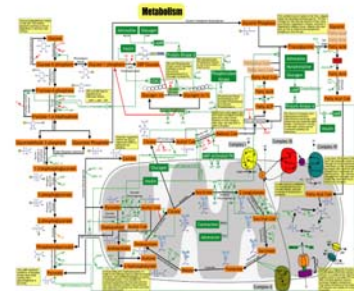
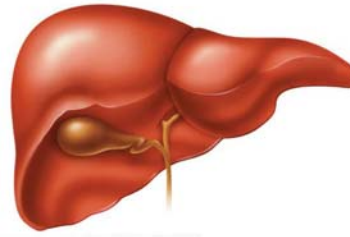
- **Use existing strengths at UTSW to establish interdisciplinary teams**
- Recruit new investigators with expertise deemed necessary to accomplish the stated goals
- Establish new Centers at UTSW to facilitate basic and translational research in obesity in the metabolic syndrome

# TORS

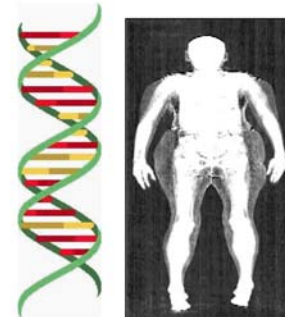
**Team 1**  
Central Regulators of  
Energy Metabolism



**Team 2**  
Molecular Biology of  
Energy Metabolism



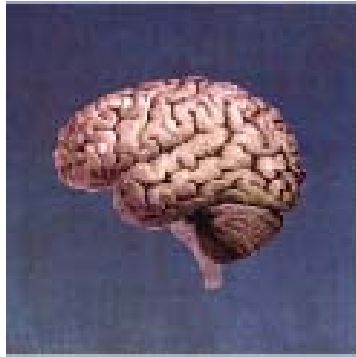
**Team 3**  
*In Vivo*  
Intermediary Metabolism



**Team 4**  
Human Genetics  
and Energy Metabolism



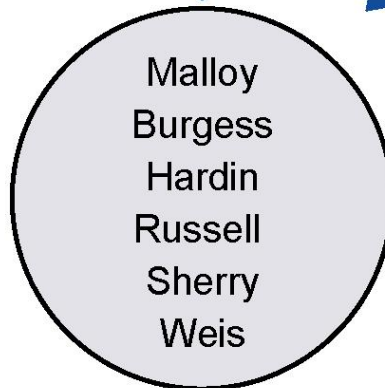
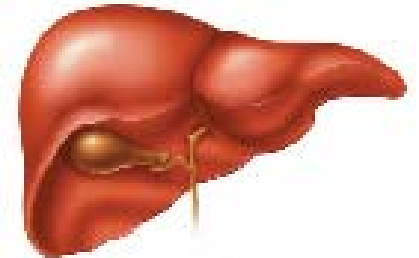
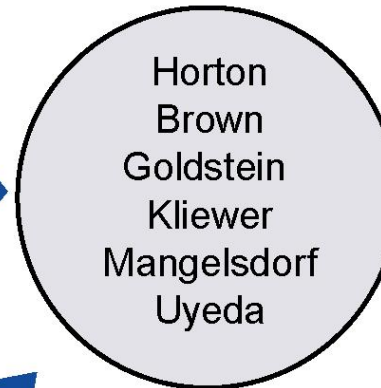




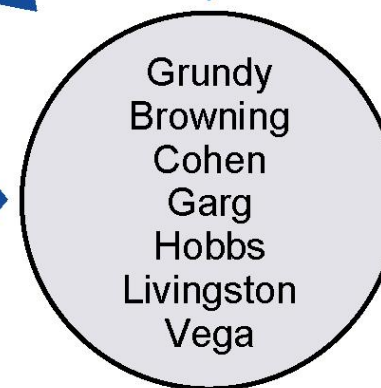
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Central Regulators of  
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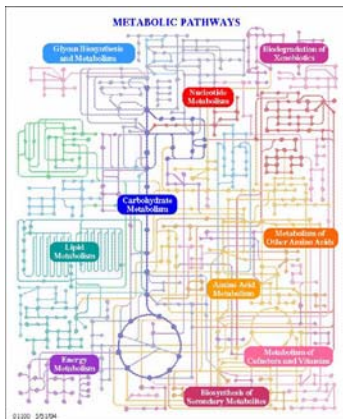
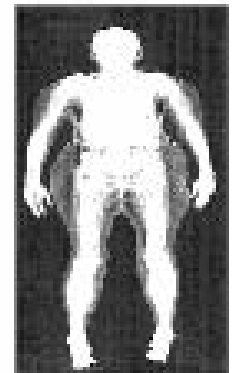
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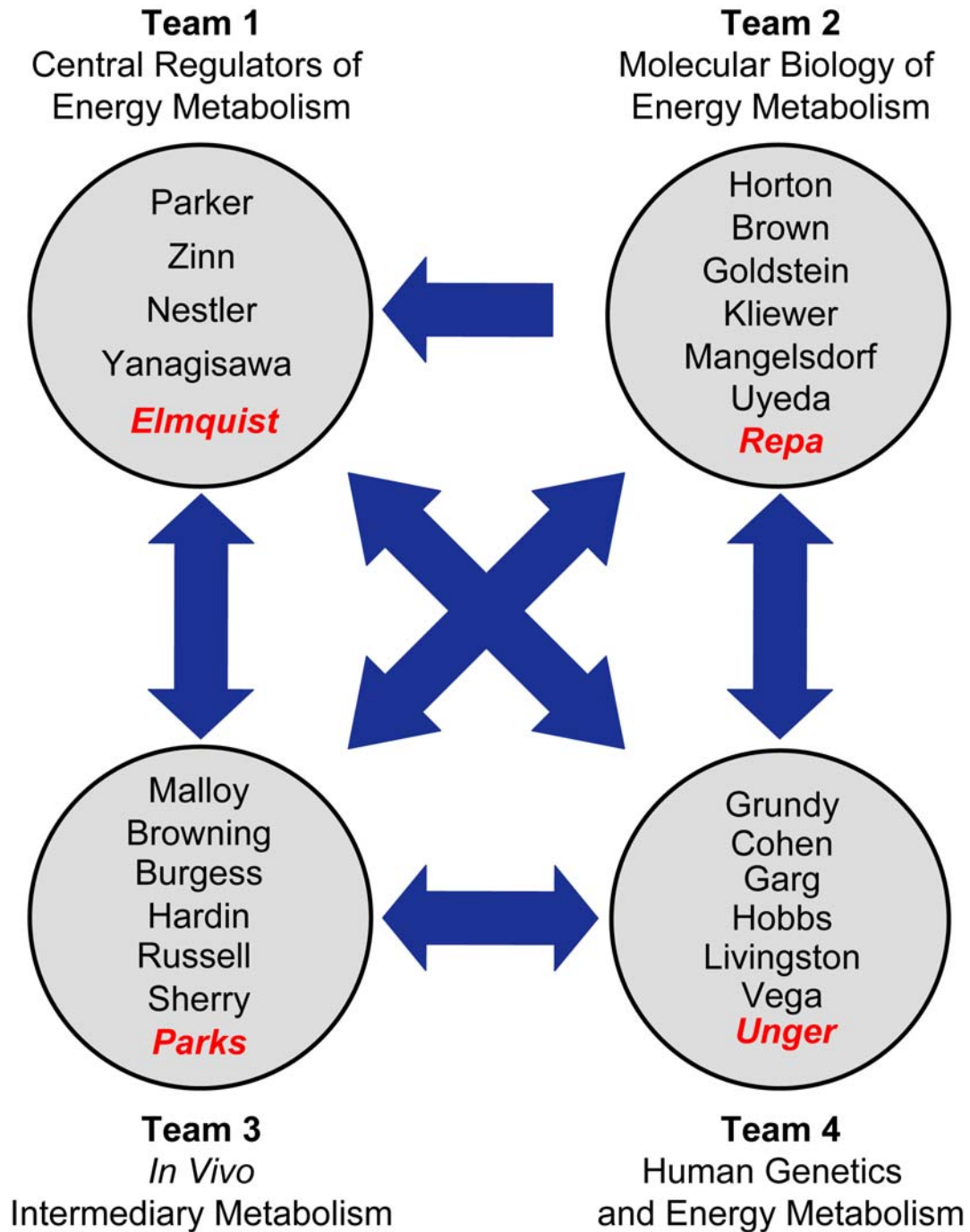


**Team 4**  
Human Genetics  
and Energy Metabolism



# Implementation

- Use existing strengths at UTSW to establish interdisciplinary teams to develop and test the central hypotheses
- **Recruit new investigators with expertise deemed necessary to accomplish the stated goals**
- Establish new Centers at UTSW to facilitate basic and translational research in obesity in the metabolic syndrome



# Implementation

- Use existing strengths at UTSW to establish interdisciplinary teams to develop and test the central hypotheses
- Recruit new investigators with expertise deemed necessary to accomplish the stated goals
- **Establish new Centers at UTSW to facilitate basic and translational research in obesity in the metabolic syndrome**

# **Implementation**

- Hypothalamic Center established**
  - Director- Joel Elmquist, Ph.D.,DVM**
  - 3 additional faculty recruits funded**
- Obesity and Diabetes Center**
  - Expansion in progress**
  - Goal is to have completed in 2006**

# Specific Objectives

- 1. Foster interdisciplinary interactions to study obesity and the metabolic syndrome**
2. Develop state-of-the-art research programs using genetically-modified mice to elucidate the metabolic and molecular bases of obesity and the metabolic syndrome
3. Support translation of scientific findings made in animal models to humans

# Foster Interdisciplinary Interactions to Study Obesity and the Metabolic Syndrome

## Team 1

Central Regulators of  
Energy Metabolism

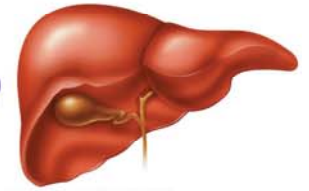


Parker (*Endocrinology/Pharmacology*)  
Elmquist (*Neuroanatomy/DVM*)  
Nestler (*Psychiatry*)  
Yanagisawa (*Molecular Genetics/Biochemistry*)  
Zinn (*Internal Medicine/Human Genetics*)

## Team 2

Molecular Biology of  
Energy Metabolism

Horton (*Gastroenterology/Molecular Genetics*)  
Brown (*Molecular Genetics/Gastroenterology*)  
Goldstein (*Molecular Genetics/Internal Medicine*)  
Kliwer (*Molecular Biology/Pharmacology*)  
Mangelsdorf (*Pharmacology*)  
Repa (*Physiology*)  
Uyeda (*Biochemistry*)



## Team 3

*In Vivo*  
Intermediary Metabolism



Malloy (*Cardiology/Radiology*)  
Browning (*Gastroenterology/Hepatology*)  
Burgess (*Radiology*)  
Hardin (*Pediatrics*)  
Russell (*Molecular Genetics*)  
Sherry (*Chemistry/Radiology*)  
Parks (*Nutrition*)

## Team 4

Human Genetics  
and Energy Metabolism

Grundy (*Internal Medicine/Nutrition*)  
Cohen (*Nutrition/Human Genetics*)  
Garg (*Endocrinology/Nutrition*)  
Hobbs (*Human Genetics/Molecular Genetics*)  
Livingston (*Surgery*)  
Unger (*Endocrinology*)  
Vega (*Nutrition*)

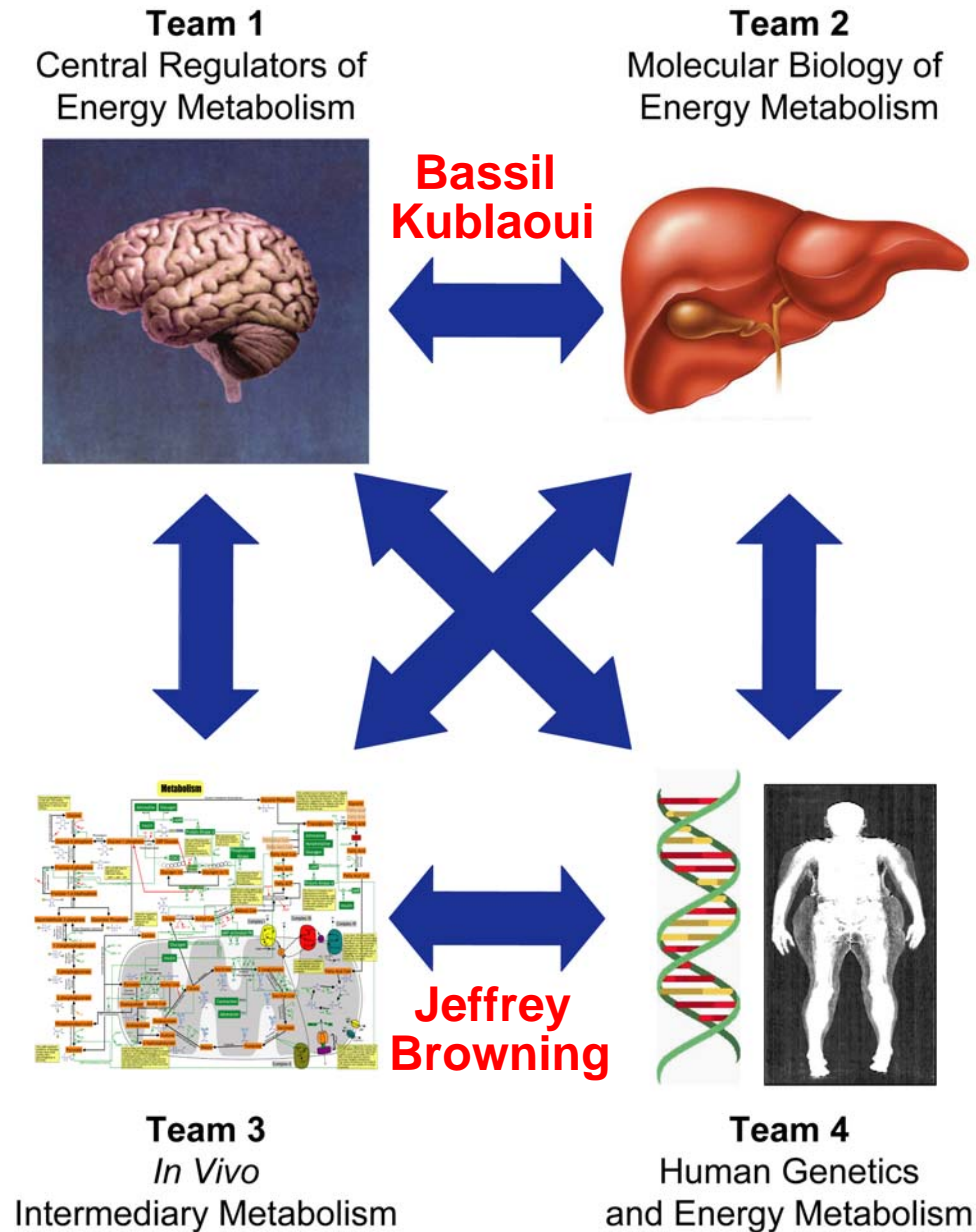


# **Objectives- Support Interdisciplinary Interactions**

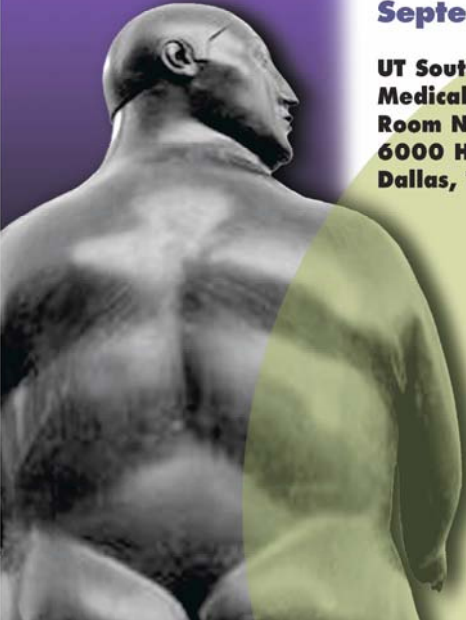
- **Initiated monthly works-in-progress meetings**
- **Support two postdoctoral fellows to work at the interface between disciplines**
- **Seminars to establish the critical questions in the field**




# Support two postdoctoral fellows to work at the interface between disciplines



# Sponsor Seminars to Establish the Critical Questions in the Field



**UT SOUTHWESTERN  
MEDICAL CENTER**



**Symposium on  
Obesity and  
Non-Esterified  
Fatty Acids**

**September 14-15, 2005**

**UT Southwestern Medical Center  
Medical Education & Conference Center  
Room NG3.112  
6000 Harry Hines Blvd.  
Dallas, TX 75234**

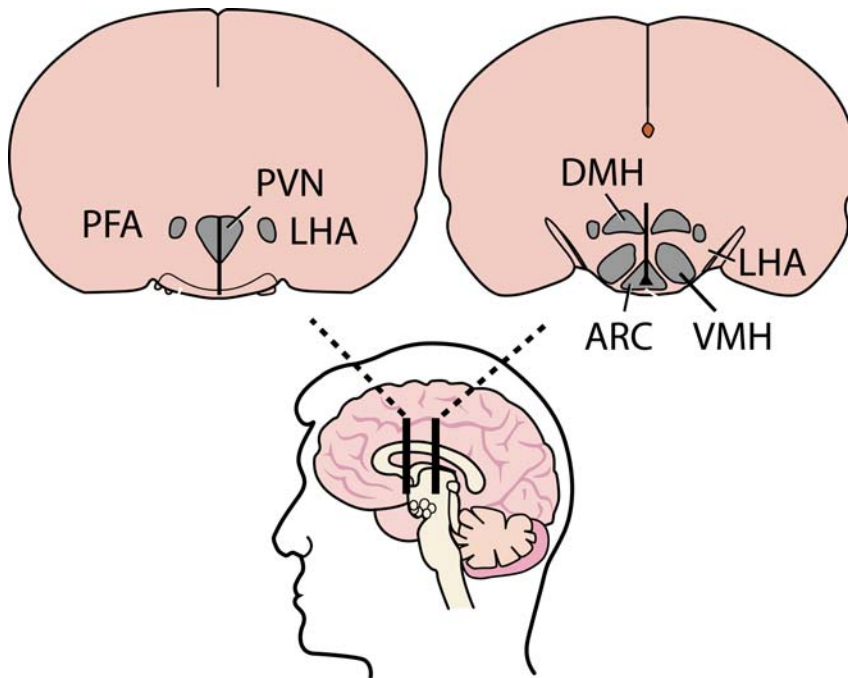
For detailed information and online registration,  
visit our website at the Center for Human Nutrition:  
<http://outside.utsouthwestern.edu/chn/nefa/index.htm>

# Specific Objectives

1. Foster interdisciplinary interactions to study obesity and the metabolic syndrome
- 2. Develop state-of-the-art research programs using genetically-modified mice to elucidate the metabolic and molecular bases of obesity and the metabolic syndrome**
3. Support translation of scientific findings made in animal models to humans

# Objectives- Research Program

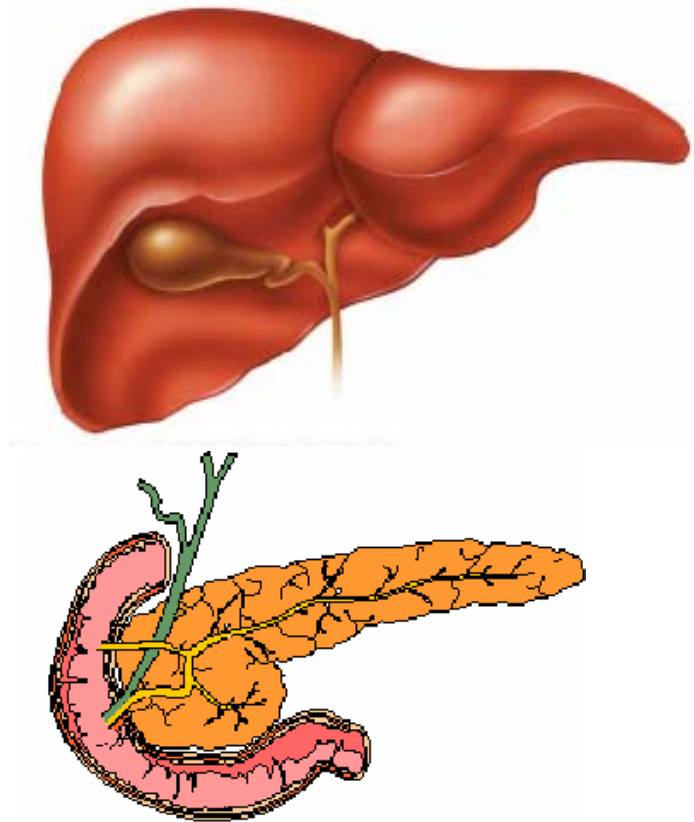
## Team 1: Central Regulators of Energy Metabolism



- Determine how regions of the hypothalamus regulate food intake and energy homeostasis
- Determine how fat-derived molecules in brain regulate energy metabolism

# Objectives- **Research Program**

## **Team 2: Molecular Biology of Energy Metabolism**



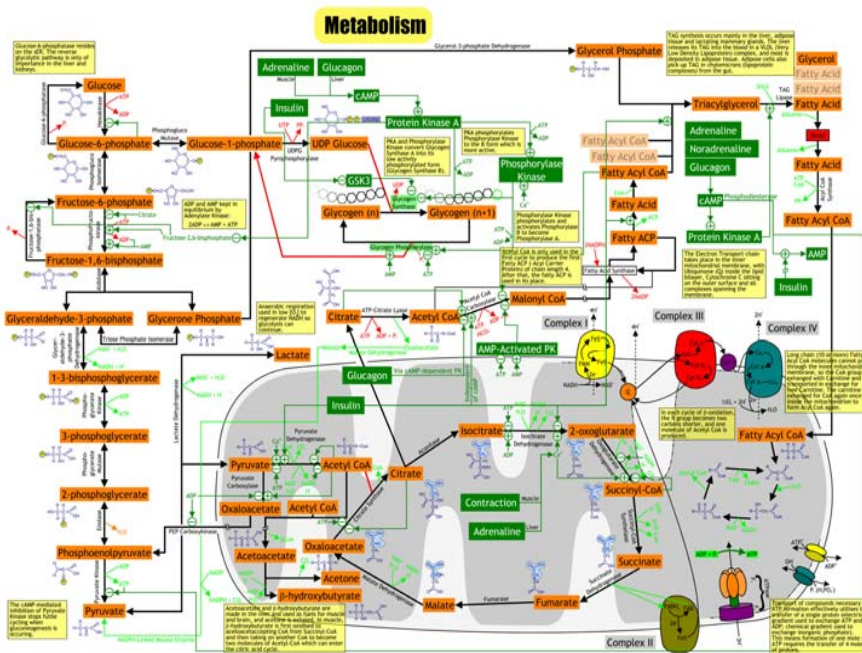
- Determine how lipids and carbohydrates influence the development of the metabolic syndrome
- Develop mice with floxed genes to study the role of lipogenesis in discrete regions of the hypothalamus and pancreas

# Specific Objectives

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# Objectives- Support translation

## Team 3: *In vivo* intermediary metabolism

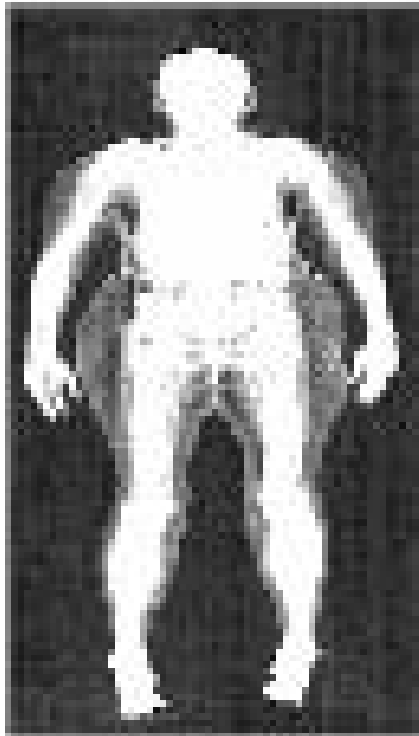


- Develop stable isotope methods to study metabolism in mice and humans
- Identify metabolic profiles for obesity and the metabolic syndrome
- Develop methods to measure glucose metabolism in mice and humans using stable isotopes
- Develop methods to measure rates of fat metabolism
- Develop tailored therapy based on metabolic profiles



# Objectives- **Support translation**

## **Team 4: Human Genetics and Energy Metabolism**



- **Build upon the unique resource at UTSW –The Dallas Heart Study (DHS)**
- **Determine how DNA sequence variations affect obesity and components of the metabolic syndrome**
- **Explore efficacy of medications for obesity and aspects of the metabolic syndrome**

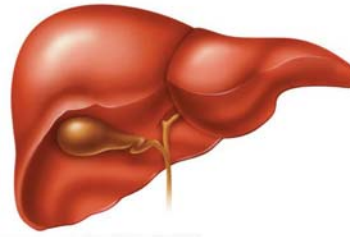


# TORS

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# Keys to Success

- **Institutional Support**
  - Area of emphasis for University
- **Importance of Scientific Problem**
- **Internal Advisory Committee**
- **Quality of Investigators**
- **Commitment of Investigators**
  - Clear scientific benefit
  - Clear monetary support

# Obstacles to Overcome

- Ensuring equal credit across disciplines
- Ensuring equal credit in promotions and tenure
  - Dean and chairman of Tenure committee have acknowledged importance of program
- Obtaining adequate funding to support a comprehensive program
  - Applying for additional federal and nonfederal funding
  - Philanthropy